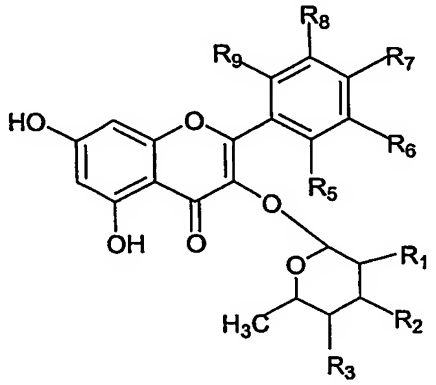
Claims

1. A pharmaceutical composition comprising

a Rsk specific inhibitor represented by the general structure:



I

wherein R_1, R_2, and R_3, are independently selected from the group consisting of hydroxy -$OCOR_4$, -COR_4 and C_1-C_4 alkoxy;

R_4 is H or C_1-C_4 alkyl; and

R_5, R_6, R_7, R_8 and R_9 are independently selected from the group consisting of H, hydroxy -$OCOR_4$, -COR_4, and C_1-C_4 alkoxy, with the proviso that R_1, R_2 and R_3 are not all hydroxy; and

a pharmaceutically acceptable carrier.

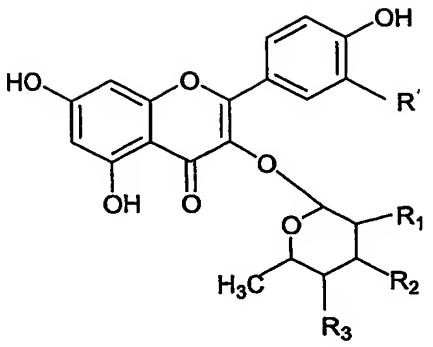
2. The composition of claim 1, further comprising an anti-tumor agent.

3. The composition of claim 2, wherein the anti-tumor agent is a chemotherapeutic.

4. The composition of claim 1 or 2, wherein R_1, R_2, and R_3, are independently selected from the group consisting of hydroxy and -$OCOR_4$.

5. The composition of claim 4 wherein R_5 and R_9 are both H and R_6, R_7, and R_8 are independently selected from the group consisting of H and hydroxy.

6. The composition of claim 1 or 2 wherein the Rsk specific inhibitor is represented by the general structure



III

wherein R is H or OH;

R_1, R_2 and R_3 are independently selected from the group consisting of hydroxy, $-OCOR_4$, $-COR_4$ and C_1-C_4 alkoxy with the proviso that R_1, R_2 and R_3 are not all hydroxy; and

R_4 is H or C_1-C_4 alkyl.

7. The composition of claim 6 wherein R is H.

8. The composition of claim 6 wherein R_1, R_2, and R_3, are independently selected from the group consisting of hydroxy and $-OCOCH_3$.

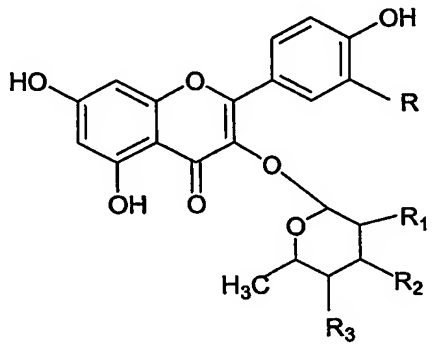
9. The composition of claims 7 or 8 wherein R_3 is $-OCOCH_3$.

10. An extract of tissues from the plant *Forsteronia refracta*, wherein said extract has Rsk specific inhibitory activity.

11. The extract of claim 10, wherein the extract is prepared by extracting tissues, selected from the group consisting of wood stem and stem bark of *Forsteronia refracta*, with a solvent comprising alcohol.

12. The extract of claim 10 wherein the extract is enriched for flavonoid compounds relative to other components present in the natural tissues.

13. A method of specifically inhibiting Rsk activity, said method comprising the step of contacting a Rsk enzyme with a compound represented by the general structure:



III

wherein R is H or OH, and R_1, R_2 and R_3 are independently selected from the group consisting of hydroxy -$OCOR_4$, -COR_4 and C_1-C_4 alkoxy; and

R_4 is H or C_1-C_4 alkyl.

14. The method of claim 13, wherein R is H or OH and R_1, R_2 and R_3 are independently selected from the group consisting of hydroxy and -$OCOCH_3$.

15. The method of claims 13 or 14 wherein R is H.

16. The method of claims 13, 14 or 15, wherein R_3 is -$OCOCH_3$.

17. A method of screening for Rsk inhibitory compounds, said method comprising the steps of

contacting a Rsk substrate with Rsk and a potential inhibitory compound under conditions that are permissive for kinase activity;

incubating the substrate for a predetermined length of time; and

determining if the substrate is phosphorylated, wherein a decrease in kinase activity relative to a reaction run in the absence of said potential inhibitory compound identifies an inhibitory compound.

18. The method of claim 17 wherein the step of determining if the substrate is phosphorylated, comprises quantitating the level of phosphorylation through the use of phosphospecific antibodies.

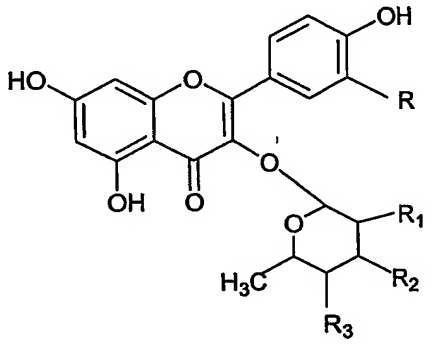
19. A method of preparing an extract that has Rsk specific inhibitory activity, said method comprising the steps of

contacting *F. refracta* tissue with an alcohol solution to produce a crude extract; and

fractionating the crude extract to isolate flavonoid compounds that exhibit Rsk specific inhibitory activity.

20. The method of claim 19 wherein the tissue comprises tissue selected from the group consisting of wood stem and bark of *F. refracta* and the contacting step comprises soaking the tissue multiple times in methanol.

21. A method for treating a disease or condition characterized by inappropriate Rsk activity, said method comprising the step of administering to a human or other mammal in need thereof, a composition comprising a compound represented by the general structure:



III

wherein R is H or OH, and R_1, R_2 and R_3 are independently selected from the group consisting of hydroxy, -$OCOCH_3$, -$COCH_3$, C_1-C_4 alkoxy, -O-glucoside and -O-rhamnoside in an amount effective for specifically inhibiting Rsk activity in the cells of said human or mammal.

22. The method of claim 21 wherein R is H and R_1, R_2 and R_3 are independently selected from the group consisting of hydroxy and -$OCOCH_3$.

23. The method of claim 21 wherein R is H or OH, R_1 and R_2 are independently hydroxy or -$OCOCH_3$ and R_3 is -$OCOCH_3$.

24. The method of claim 23 wherein R is H.

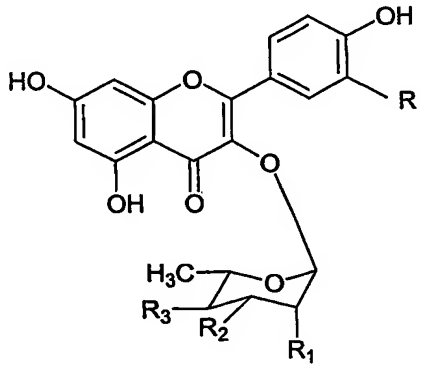
25. A method for treating a disease or condition characterized by inappropriate Rsk activity, said method comprising the step of administering to a patient in need thereof a composition comprising a Rsk specific inhibitor.

26. The method of claim 25 wherein the Rsk specific inhibitor comprises a compound selected from the group consisting of an anti-sense oligonucleotide and an interfering oligonucleotide.

27. The method of claim 25 wherein the Rsk specific inhibitor comprises an interfering oligonucleotide directed against Rsk1, Rsk2, Rsk3 or Rsk4.

28. The method of claim 25 wherein the Rsk specific inhibitor comprises an extract from the tissues of *Forsteronia refracta* or *Zingiber zerumbet.*

29. The method of claim 25 wherein the Rsk specific inhibitor comprises a compound represented by the general structure:



II

wherein R is H or OH, and R_1, R_2 and R_3 are independently selected from the group consisting of hydroxy -$OCOR_4$, -COR_4, C_1-C_4 alkoxy, -O-glucoside and -O-rhamnoside, and R_4 is H or C_1-C_4 alkyl.

30. The method of claim 29, wherein R is H or OH and R_1, R_2 and R_3 are independently selected from the group consisting of hydroxy and -$OCOCH_3$.

31. The method of claims 25-28 or 30 wherein the disease is a neoplastic disease.

32. The method of claim 31 further comprising the steps of administering said patient anti-tumor therapy.

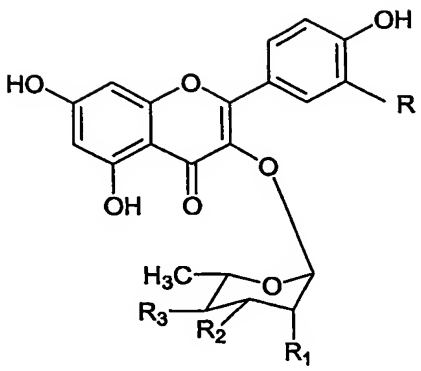
33. A composition comprising a Rsk specific inhibitor and an anti-tumor agent.

34. The composition of claim 33 wherein the Rsk specific inhibitor is selected from the group consisting of an anti-sense oligonucleotide and an interfering oligonucleotide.

35. The composition of claim 34 wherein the Rsk specific inhibitor comprises an interfering oligonucleotide directed against Rsk1, Rsk2, Rsk3 or Rsk4.

36. The composition of claim 33 wherein the composition comprises an extract from the tissues of *Forsteronia refracta* or *Zingiber zerumbet* as a source of the Rsk specific inhibitor.

37. The composition of claim 33 wherein the Rsk specific inhibitor comprises a compound represented by the general structure:



II

wherein R is H or OH, and R_1, R_2 and R_3 are independently selected from the group consisting of hydroxy -$OCOR_4$, -COR_4, C_1-C_4 alkoxy, -O-glucoside and -O-rhamnoside, and R_4 is H or C_1-C_4 alkyl.

38. The composition of claim 37, wherein R is H or OH and R_1, R_2 and R_3 are independently selected from the group consisting of hydroxy and -$OCOCH_3$.

39. A diagnostic method for detecting neoplastic cells, said method comprising the steps of

measuring a Rsk quantification factor, selected from the group consisting of Rsk nucleic acid quantity, Rsk protein quantity or Rsk enzymatic activity, in a biological sample isolated from an individual; and

determining if the Rsk quantification factor is elevated relative to a standard, wherein an elevated Rsk quantification factor detected in said biological sample indicates the presence of neoplastic cells.

40. The method of claim 39 wherein the biological sample comprises cells recovered from a biopsy.

41. The method of claim 39 wherein the standard comprises a corresponding non-Rsk nucleic acid quantity, non-Rsk protein quantity or non-Rsk enzymatic activity detected in said biological sample.

42. The method of claim 39 wherein the standard comprises a corresponding Rsk nucleic acid quantity, Rsk protein quantity or Rsk enzymatic activity detected in healthy tissue of said individual.

43. The method of claim 39 wherein the standard comprises a corresponding Rsk quantification factor detected in a reference biological sample obtained from healthy tissue.

44. The method of claim 39 wherein the measured Rsk quantification factor is Rsk activity, and the step of measuring the Rsk activity comprises isolating Rsk protein from said biological sample and conducting *in vitro* kinase assays

45. The method of claim 39 wherein the measured Rsk quantification factor is Rsk protein quantity and the step of measuring the quantity of Rsk protein comprises

contacting the Rsk protein with an antibody specific for Rsk protein, wherein the antibody is labeled;

removing the non-bound and non-specific antibody; and

quantifying the amount of label remaining to determine the amount of Rsk protein present.

46. The method of claim 39 wherein the measured Rsk quantification factor is Rsk nucleic acid quantity and the step of measuring the quantity of nucleic acid comprises

contacting the nucleic acids of the biological sample with a labeled Rsk complementary nucleic acid probe;

removing the non-bound and non-specific probe; and

quantifying the amount of label remaining to determine the amount of Rsk nucleic acid present in the biological sample.

47. A composition comprising a Rsk inhibitor isolated by the steps of

extracting tissues, selected from the group consisting of wood stem and stem bark of *Forsteronia refracta*, with a methanol solution;

applying the extracted material to a polyamide 6S column;

washing successively with H_2O, 1:1 H_2O-MeOH, 9:1 CH_2Cl_2-MeOH and 1:1 CH_2Cl_2-MeOH to afford four fractions;

recovering the 1:1 CH_2Cl_2-MeOH fraction;

applying the1:1 CH_2Cl_2-MeOH fraction to a diol gel column;

washing successively with CH_2Cl_2, 99:1 CH_2Cl_2-MeOH, 95:5 CH_2Cl_2-MeOH, 90:10 CH_2Cl_2-MeOH and MeOH to give five fractions;

combining the 99:1 CH_2Cl_2-MeOH, 95:5 CH_2Cl_2-MeOH and 90:10 CH_2Cl_2-MeOH fractions to isolate a composition comprising a Rsk inhibitor.